

WHAT IS CLAIMED IS:

1. An isolated mutant cell comprising decreased levels of sialic acid containing host cell receptors for influenza virus relative to a corresponding wild-type cell which supports efficient influenza virus replication.
2. The isolated mutant cell of claim 1 which is a mammalian cell.
3. The isolated mutant cell of claim 2 which is a swine, bovine, simian or canine cell.
4. The isolated mutant cell of claim 1 wherein the wild-type cell is a MDCK cell.
5. The isolated mutant cell of claim 2 which is a mink cell.
6. The isolated mutant cell of claim 5 which is a mink lung cell.
7. The isolated mutant cell of claim 1 which is an avian cell.
8. The isolated mutant cell of claim 1 which has decreased levels of *N*-acetylneuraminic acid.
9. The isolated mutant cell of claim 1 which has decreased levels of *N*-glycolylneuraminic acid.
10. The isolated mutant cell of claim 1 which has decreased levels of *N*-acetylneuraminic acid and *N*-glycolylneuraminic acid.

2022-04-20 10:50:00 AM - 2022-04-20 10:50:00 AM

11. The isolated mutant cell of claim 1 which has at least ten fold lower levels of *N*-acetylneuraminic acid and at least 2 fold lower levels of *N*-glycolylneuraminic acid relative to the corresponding wild-type cell.
12. A method to isolate a cell that has decreased levels of receptors for influenza virus, comprising:
 - a) contacting a population of cells permissive for influenza virus replication and sensitive to lectin or agglutinin growth inhibition with an amount of lectin or agglutinin so as to yield cells that are resistant to growth inhibition by the lectin or agglutinin, wherein the lectin or agglutinin specifically binds sialic acid; and
 - b) isolating a lectin- or agglutinin-resistant cell having decreased levels of receptors for influenza virus.
13. The method of claim 12 wherein the lectin is *Maakia amurensis* lectin.
14. The method of claim 12 wherein the lectin is *Sambucus nigra* lectin.
15. The method of claim 12 wherein the agglutinin is *Limax flavus* agglutinin.
16. The method of claim 12 wherein the lectin is *Tritrichomonas mobilensis* lectin.
17. The method of claim 12 wherein the lectin specifically binds sialic acid linked to galactose by α (2-3) or α (2-6) linkages.
18. The method of claim 12 wherein the lectin specifically bind sialic acid linked to *N*-acetylgalactosamine by α (2-6) linkages.
19. The method of claim 12 wherein the cells are mammalian cells.

100077-022002

20. The method of claim 19 where the cells are canine, swine, bovine, mink, human or simian cells.
21. The method of claim 12 wherein the population of cells is a population of MDCK cells.
22. A resistant cell isolated by the method of claim 12.
23. The cell of claim 22 which is resistant to growth inhibition by *Maakia amurensis* lectin or *Sambucus nigra* lectin.
24. The cell of claim 22 which is resistant to growth inhibition by *Maakia amurensis* lectin and *Sambucus nigra* lectin.
25. A method of propagating influenza viruses having reduced sialidase activity, comprising: contacting the mutant cell of claim 1 or the resistant cell of claim 22 with an amount of an influenza virus having reduced sialidase activity so as to yield progeny virus.
26. Progeny virus obtained by the method of claim 25.
27. A method of using a host cell having decreased levels of sialic acid containing host cell receptors for influenza virus, comprising:
 - a) contacting the isolated mutant cell of claim 1 or the resistant cell of claim 22 with an amount of an influenza virus having substantially wild-type levels of sialidase activity so as to yield progeny virus; and
 - b) serially propagating the progeny virus with the mutant cell of claim 1 or the resistant cell of claim 22 so as to yield adapted viruses which efficiently

replicate in the mutant cell, the lectin-resistant cell or the agglutinin-resistant cell.

28. The method of claim 27 further comprising isolating the adapted virus.
29. Isolated adapted virus obtained by the method of claim 27 which adapted virus does not have a mutation in the HA gene relative to the virus having substantially wild-type levels of sialidase activity.
30. The method of claim 25 or 27 wherein the influenza virus is type A influenza virus.
31. The method of claim 25 or 27 wherein the influenza virus is type B influenza virus.

00000000000000000000